

Claims 1-10, 13-22, and 59-63 stand rejected under Section 103(a) based on Carr *et al.*, and claims 1-22 and 59-63 stand rejected under Section 103(a) based on Carr *et al.* in view of Girot *et al.* The examiner urges that "Carr *et al.* discloses dense mineral oxide supports comprising a mineral oxide matrix and an interactive polymer network which is rooted in pores and on the surface of the mineral oxide matrix (see abstract). It is unclear what 'rooted in the pores' means as discussed above. However, it is considered that the network of Carr *et al.* ('373) would intrinsically enter intricacies to at least some extent."

In the first instance, the term "rooted in pores" clearly defines a surface layer of polymer that can interact with desired macromolecules and that is held stably in place because it is part of a network that is rooted in the pores of the media. Thus, the paragraph bridging pages 9 and 10 of the specification describes that:

the pore volume is left just large enough to allow polymers to be rooted in the pores, and these rooted polymers layer on the external surface of the beads where the interaction with the macromolecules occurs. The resulting layer of polymers, or interactive polymer network, is stable and remains in place. The interaction of the desired molecules occurs on the external surface area of the beads due to the rooted polymers.

The abstract of Carr *et al.* does *not* disclose "a mineral oxide matrix and an interactive polymer network which is rooted in the pores." The abstract of Carr *et al.* discloses a stable stationary phase for chromatography which comprises porous ZrO<sub>2</sub> spherules coated with a cross-linked polymer coating." There is no disclosure in the remainder of the Carr document to suggest a mineral oxide matrix with an interactive polymer matrix rooted in the pores as claimed by applicants. Carr discloses two embodiments. A first embodiment relates to ZrO<sub>2</sub> spherules prepared by dispersing an aqueous sol of colloidal ZrO<sub>2</sub> particles in a medium which extracts water from the dispersed sol to produce gelled ZrO<sub>2</sub> spherules which are then heated to yield porous ZrO<sub>2</sub> (column 4, lines 47-58). In an alternative embodiment, the porous ZrO<sub>2</sub> spherules are coated with a hydrophobic or hydrophilic, crosslinked polymer.

There is nothing in this description to suggest that the polymer network is rooted in the pores of the mineral oxide matrix. To the contrary, the emphasis in Carr is on large pore diameters and pore volume, in clear contrast to the present invention which uses a pore volume

of less than 30%, one that is “just large enough to allow polymers to be rooted in the pores.” Applicants’ claimed pore volume is intrinsically related to the recitation of an interactive polymer network rooted in the pores. The allegation that the polymer coating of Carr *et al.* might “intrinsically enter intricacies to at least some extent” does not support a conclusion that the polymer is “rooted in the pores” as in applicants’ novel and inventive media. The preferred large pore diameter and pore volume in Carr effectively counters such a conclusion.

The examiner goes on to state that:

The lowest porosity explicitly disclosed is 31%, which occurs at a sintering temperature of 900 degrees. It is considered that it would have been obvious to one of ordinary skill in the art to have made the porosity <30%. Carr *et al.* (‘373) discloses the (sic: “that”?)’the surface area and pore volume decrease with increasing firing temperature’ (col. 13, lines 37-39) and also that the sintering temperature can range from 100-1500 degrees (col. 8, lines 20-29). This would suggest to one of ordinary skill in the art to decrease the porosity below 30%.

For both embodiments, the teaching of Carr *et al.* is that pore volume should be *maximized*, not controlled to values of porosity of less than 30% as presently claimed. The increased pore diameter is desired to allow the proteins which are to be separated to diffuse freely into the internal void volume, thereby reaching all available surface area. Thus, Carr *et al.* states that “the data summarized in Table 1 show that it is possible *to increase the average pore diameter* by increasing the firing temperature from 400° to 900°C. The surface area and pore volume decrease with increasing firing temperature. Chromatographic activity of the ZrO<sub>2</sub> spherules is determined by the parameters of the surface area, average pore diameter and pore volume. Accordingly, the appropriate firing temperature is selected.”

Similarly, Carr discloses that a colloid size should be chosen which *maximizes* porosity and pore diameter. For example, Carr states that “the data summarized in Table II show that it is possible to control the average pore diameter of the fired spherules by appropriate selection of the colloid size of the ZrO<sub>2</sub> source. Larger colloids produce fired spherules with *larger pore diameters and pore volumes*” (column 14, lines 1-5).

The examples of Carr clearly select firing temperature and colloid size so as to maximize porosity and pore size, typically by using a firing temperature of 600°C. A further emphasis on *increasing* porosity and pore size is found in Example 8, which discloses that “centrifugation, removal of the supernatant, and redispersion of the colloidal ZrO<sub>2</sub> starting material results in increases in the average pore diameter, pore volume and surface area of the fired spherules...regardless of mechanism, the centrifugation treatments describes in Examples 6-8 provide a method of preparing spherules with increased average pore diameter, pore volume and surface area relative to spherules prepared from untreated colloidal ZrO<sub>2</sub> sols.”

The examples which relate to coated particles all use particles prepared according to Example 2. Example 2 fires the ZrO<sub>2</sub> spherules at 600°C. As shown in Table 1, these particles have a pore volume of 36%. There is no suggestion to fire at a higher temperature in order to reduce this pore volume. Indeed, as noted above, *the clear suggestion in Carr et al. is that pore volume and pore size should be maximized.* Accordingly, there is no suggestion to modify the firing temperature to be used in order to produce a matrix with a pore volume of less than 30% as presently claimed.

Indeed, a modification of Carr to decrease pore size and volume would be contrary to the teaching of the reference. If a proposed modification renders a prior art invention unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. “The question is . . . whether it would have been obvious from a fair reading of the prior art reference as a whole to . . . [modify the reference] . . . The mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification.” *In re Gordon*, 221 USPQ 1121, 1127 (Fed. Cir. 1984). See also MPEP §2143.01. In analyzing the prior art, it is impermissible to “pick and choose from any one reference only so much of it as will support a given position, to the exclusion of the other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.” *In re Wesslau*, 353 F.2d 238, 241, 147 USPQ 391, 393 (CCPA 1965). “Whether a particular combination might be ‘obvious to try’ is not a legitimate test of patentability.” *In re Fine*, 837 F.2d 1071, 1075 5 USPQ2d 1596, 1599 (Fed. Cir. 1988).

Applicants produce particles with low porosity by firing at high temperatures, in the range of 900°C to 1500°C, and preferably between 1000°C and 1400°C, so as to melt the submicroparticles together and reduce the particle diameter and reduce the pore volume to less than about 30%. This low porosity material is essential to firmly anchor the interactive polymer network on the beads - to provide a polymer network that is “rooted in the pores” as claimed. Carr *et al.* teaches away from a pore volume of less than 30% as recited in applicants’ claims. As a general rule, a prior art reference that teaches away cannot serve to create a *prima facie* case of obviousness. *In re Gurley*, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994). Regarding teaching away, a prior art reference is said to teach away from the claimed invention when “a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.” *Id.* Teaching away is a *per se* demonstration of lack of *prima facie* obviousness. *In re Dow*, 5 USPQ2d 1596 (Fed. Cir. 1988). The path taken by applicants diverges from that suggested of Carr *et al.*, by using a mineral oxide matrix with a pore volume of less than 30%.

The issue of obviousness is determined entirely with reference to a hypothetical person having ordinary skill in the art. *Standard Oil Co. v. American Cyanamid Co.*, 774 F.2d 448, 454, 227 USPQ 293, 297-98 (Fed. Cir. 1985). Furthermore, in considering the person of ordinary skill in the art, that hypothetical person is “presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate . . . .” *Id.* Therefore, persons of ordinary skill are guided by conventional wisdom. *W.L. Gore & Assoc.*, 721 F.2d 1540, 1553, 220 USPQ 303 (Fed. Cir. 1983). In Carr *et al.*, the “conventional wisdom” is to *increase* porosity, not to make a mineral oxide matrix which has a pore volume of less than 30%.

Giroi *et al.* is added for a teaching of polysaccharide organic polymers as the material of the polymer network. Giroi *et al.* does not overcome Carr’s failure to suggest a matrix with a porosity of less than 30% in which an interactive polymer network is rooted.

In view of the foregoing remarks, it is believed that all claims are in condition for allowance. Reconsideration of all rejections and a notice of allowance are respectfully requested. Should there be any questions regarding this application, the examiner is invited to contact the undersigned attorney at the phone number listed below.

Respectfully submitted,

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